REMARKS

In the Action, several objections in earlier Office Actions were withdrawn and such action is noted and appreciated. At this time, only claims 17-28 remain in the case, with only claim 17 being independent.

All of the rejections of the claimed subject matter based on prior art references have been either withdrawn or overcome. The only remaining rejections of the claims are §112 rejections. More specifically, claims 17-28 stand rejected under 35 U.S.C. §112, first paragraph, for a number of reasons. In addition, all of the claims stand rejected under second paragraph 35 U.S.C. §112 mainly due to inclusion of the term "immunomodulatory" in claim 17.

The Applicant has spent considerable time and effort in analyzing the Examiner's comments and submits that the following remarks and attached exhibits overcome all of the remaining objections.

First, it is submitted that all of the claims have been amended slightly in order to make them clearer and to obviate some of the Examiner's objections. Favorable review and allowance of amended claims 17-28 is solicited.

(1) The Examiner contends that the examples set forth in the specification (pages 22-24) are insufficient to show that the claimed vaccine complex could be effective in "treating or preventing" disease or "how it can be made." In response, the Examiner is advised that "prevention" of the disease is not an object of the invention and

the specification is only directed to treatment of the anti-bio-resistant strain. Thus, any data regarding "prevention" is unnecessary.

The Applicant has not described epidemiology studies on this ground, but has only indicated in Example 2 degeneration of a gastritis into an ulcer and in Example 1 the extension of a gastritis into an esophagitis. It is submitted that the four examples set forth in the specification adequately describe how the diagnosis was established and how the control of the cure was achieved. Regarding the therapeutic protocols, they are described and their ratios appear on pages 19-22.

The process for producing the vaccine complex is similar to that described in Applicant's recently issued U.S. Patent No. 6,503,512 (apart from Helicobacter). It is submitted that since the U.S. '512 patent has a similar-type of disclosure as the present application and was allowed by the Patent Office, that it would be inconsistent to maintain the §112 objections in this case.

Processes for producing vaccine complexes are also shown in "Guide to Molecular Cloning Techniques" in Method in Enzymology, Vol. 152 (See Section VII) (Exhibit A); Isolation of Ribosomal Subunits Containing Intact rRNA from Human Placenta: Estimation of Functional Activity of 80S Ribosomes," Analytical Biochemistry, 219-223 (1991) (Exhibit B); "Defined Media for H. pylori," in Methods in Molecular Medicine (Exhibit C); and "Molecular Characterization of H. pylori Surface Antigens" in Methods in Molecular Medicine (Exhibit D).

(2) The Examiner indicates that the specification (page 3) mentioned the "inefficacy" of Helicobacter-specific antibodies in the treatment of diseases. This is correct only with respect to vaccines based only on Helicobacter. See "Vaccination of Gnotobiotic Piglets against Helicobacter pylori" in Journal of Infectious Diseases (1998) (Exhibit E).It is the complement which is essential to immunity. See "Biochemistry Illustrated" pp. 65, 69 (Exhibit F).

The present invention is unique in the scientific field of research as the amino acid in the Collagen Type III represents the anti-genecity required. (Compare the coupling of an amino acid arm ensuring binding to a target with a genetic RNA arm – page 24, lines 4-16.)

(3) As to the Examiner's question concerning the Type III Collagen, it is believed that the answer is set forth sufficiently in the specification. More specifically, the Type III Collagen comprises all of the essential amino acids apart from the Tryptophan and has the following characteristics (see page 13 of the specification):

(a) The collagen is from gastro intestinal tractus;

(b) The amino acids are listed; and

(c) The amino acids are quantified.

The other characteristics of Type III Collagen are either listed in the specification or known to persons skilled in the art. See "Structure, Molecular Biology and Pathology of Collagen" in Annals of the New York Academy of Sciences, Vol. 580 (1990) (Exhibit

G). Any of the amino acids listed in claim 18, or mixtures thereof, can be utilized as the Type III collagen in the inventive vaccine complex. There is no undue experimentation needed.

(4) As to the RNAs and RNA fragments referred to on page 5 (top) of the Office Action, the Examiner is referred to pages 4-5 of the specification. The sources of the membrane fractions are stated on pages 5-12 of the specification. The collagen Type III can be of human, bovine, or fish origin.

The antibiotics to which the disease or the bacteria has become resistant to are those which are described in most international protocols or in technical literature in the relevant art. See "Helicobacter Pylori – From Bench to Bedside" in the Canadian Journal of Gastroenterology (1997) (Exhibit H).

(5) The optimal amounts or proportions of the complex components are well described in the specification: intravenous injections (p. 20); subcutaneous injections (p. 20); oral (p. 21); transdermic (pps. 21-22). It is believed that the written description in the specification is adequate for persons skilled in the art to practice the invention. It is not necessary for all ranges of all components be included so long as the invention can be practiced without undue experimentation.

(6) With regard to the applicant's Exhibits, the Examiner is directed to "Perspectives of anti-H. pylori vaccination" in J. Physiol Pharmacol 1997 (Exhibit I). So long as there are well-established methods for diagnosis of Helicobacter Pylori, it is not

meaningful whether it is the "gold-standard" or a lesser-standard. Persons of skill in the art would be able to use these standards and predict if protective immunity had been induced.

(7) The Examiner's comment concerning the effect of the absence of animal data and the alleged "insufficiency" of showing effectiveness and how the claimed vaccine complex could be made, are unsupported and should not be legitimate grounds for denying patentability of the present invention. Simply because the vaccine complex is new and has not been tested in a manner believed necessary by the Examiner does not mean that the invention is not significant or an important contribution to the art. The examples set forth in the specification are significant and have been extracted from different serological studies as well as different clinical trials. See "Animal Models for Host-Pathogen Interaction Studies" in British Medical Bulletin (1998) (Exhibit J) and "Animal Studies and Vaccines" in GVT (Exhibit K).

Further, the issue of "preventing" is not applicable. The present invention was not mentioned as a preventative treatment, on a population, on bacteriological grounds, but only as a curing treatment and dispensing with recidivations. All of the described therapeutic protocols are in relation to the confirmation rate (e.g. subcutaneous injection, intravenous, oral, etc.). The protocols are a function of each clinical type.

(8) As to Rappouli et al., it is noted that no side effects were observed. It was well known at the time of the invention that the complex components did not induce any

side effects when injected in humans. In the Applicant's clinical experiments, none were ever incurred. See Pediatric Infectious Disease Journal (1998) (Exhibit L). As for the bacterium extract and RNA membrane fraction, the eventual vaccine effects which could have happened when instant vaccine was injected, have been pre-empted with the adjunction of Betamethazene Disodium Phosphate. See "Collagen" in Martindale (1996) (Exhibit M).

(9) As to prior Exhibit C, a copy of the correct Abstract is attached hereto, now as Exhibit N. The Examiner is requested to consider this reference together with the Applicant's comments relative to it in the previous responsive amendment.

(10) In summary, the Applicant's scientific projections have been corroborated in recent publications concerning the interferent RNA. See the three articles attached hereto collectively as Exhibit O. In each form of the instant vaccine, the delivery included quantitative and qualitative data on proteoglycans of saccharidic membrane fractions, 5 RNA extracted from 5 different bacteria's strain, and the exact quantity of Collagen Type III, as well as the quantity of a major anti-inflammatory needed for diminishing the potential inflammatory phenomenon and prevent any eventual side effects i.e. potential vaccinal reaction. The Type III Collagen of the instant application is a key element in the complement genesis. All of these elements were not known by any person skilled in the art when the instant application was first filed.

Also, the Examiner should note that the interferent RNA has been recognized as a new biological continent.

(11) As to the Examiner's objection to the term "immunomodulatory," the references show that "immunomodulatory" and its related terms were all well known and defined in the art, and were known and defined long before the date of the Applicant's invention. See Exhibit P.

However, in an effort to reduce the issues and prepare the case for allowance, all of the claims have been amended to substitute "immunodulatory" for "immunomodulatory."

(12) As to claim 18, the Examiner is referred to item "(3)" above. The Type III collagen can consist of only a single amino acid from the recited group, although mixtures of two or more amino acids are preferred.

(13) As to claim 19, the Examiner is referred to pages 20-21 of the specification. It is Helicobacter Pylori.

Finally, the Examiner is requested to take into account that the present invention not only has been successful in clinical trials, but is a significant and important contribution to the field. As stated in "A. H. Pylori Vaccine is Essential" (2000) (Exhibit Q):

> "Multivalent vaccines can be required for successful protection against H. Pylori in humans . . .
>
> * * *

> Alternate routes of vaccine administration ...in humans...
>
> * * *
>
> Potentially toxic adjuvants may not be required, but it deemed necessary to modulate the immune response..."

It is also noteworthy to point out that patent protection from the same application and specification has been allowed and/or issued in several other countries, including Australia (AU 722200) and China (CN 1089607C).

Further, the fact that U.S. Patent No. 6,503,512 issued to the Applicant on a related invention with a similar specification is material to the present analysis. In the U.S. '512 patent, the structure and fabrication process of a non-specific immunomodulatory complex are described.

In view of the foregoing, it is submitted that all of the claims remaining in the case, namely claims 17-28, are in proper form and patentably distinguish from the prior art. Additionally, it is believed that the subject matter of all of the claims is patentable under the standards of 35 U.S.C. §112 for the reasons as stated above.

Accordingly, allowance of the claims and passage of the application to issuance are respectfully solicited.

Respectfully submitted,

John A. Artz
Registration No. 25,824
28333 Telegraph Road, Suite 250
Southfield, Michigan 48034
Phone: (248) 223-9500
Fax: (248) 223-9522

Dated: June 9, 2003

"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

In the Claims:

Please replace claims 17-28 with the following:

17. (Twice Amended) An [immunomodulatory] immunodulatory and *anti-Helicobacter-specific* vaccine complex comprising:

(a) ribosomal ribonucleic acid extracted from bacteria selected from the group consisting of: *Helicobacter pylori, Helicobacter hepaticus, Helicobacter coronari,* or a mixture thereof;

(b) the amino acids of the [a] type III collagen; and

(c) bacterial membrane fractions containing glycopeptides and/or lipopolysaccharides.

18. (Twice Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 17 wherein the type III collagen comprises amino acids selected from the group consisting of aspartic acid, hydroxyproline, threonine, serine, glutamic acid, proline, glycine, alanine, valine, methionine, isoleucine, leucine, tyrosine, phenylalanine, lysine, histidine, arginine, and mixtures thereof.

19. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 17 for use in the treatment of diseases caused by *Helicobacter* bacteria, by the production of antibodies and the production of endogenous interferon.

20. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 18 for use in the treatment of diseases caused by *Helicobacter* bacteria, by the production of antibodies and the production of endogenous interferon.

21. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 17, for use as an anti-idiotype vaccine against the idiotype of anti -*Helicobacter sp.* antibodies which make it possible to avoid recidivations of the

initial digestive tract pathology caused by *Helicobacter sp.*

22. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 18, for use as an anti-idiotype vaccine against the idiotype of anti -*Helicobacter sp.* antibodies which make it possible to avoid recidivations of the initial digestive tract pathology caused by *Helicobacter sp.*

23. (Twice Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 17, for use against antibiotic-resistant *Helicobacter* bacteria resistant to conventional treatments.

24. (Twice Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 18, for use against antibiotic-resistant *Helicobacter* bacteria resistant to conventional treatments.

25. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 17 wherein the said complex is formulated in such a way that it enables simultaneous administration of the said complex together with substances selected from the group consisting of corticosteroids, antibiotics, antisecretory agents such as proton pump inhibitors, products with bacteriostatic effect, products with bactericidal effect and products with anti-inflammatory effect.

26. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 18 wherein the said complex is formulated in such a way that it enables simultaneous administration of the said complex together with substances selected from the group consisting of corticosteroids, antibiotics, antisecretory agents such as proton pump inhibitors, products with bacteriostatic effect, products with bactericidal effect and products with anti-inflammatory effect.

27. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 25 wherein the said complex is formulated in such a way that it enables administration of the said complex by a route selected from intravenous route, subcutaneaous route, transdermal route and per os.

28. (Amended) The [immunomodulatory] immunodulatory and vaccine complex according to claim 26 wherein the said complex is formulated in such a way that it enables administration of the said complex by a route selected from intravenous route, subcutaneaous route, transdermal route and per os.